Supplementary Table 1. Baseline Disease Characteristics (Safety Population)

	MTX				
	10 mg (n=13)	**15 mg (n=12)**	**20 mg (n=12)**	**25 mg (n=12)**	**Overall (N=49)**
ACR RA classification, n (%)					
Stage I	2 (15.4)	0 (0.0)	0 (0.0)	1 (8.3)	3 (6.1)
Stage II	5 (38.5)	6 (50.0)	11 (91.7)	8 (66.7)	30 (61.2)
Stage III	6 (46.2)	5 (41.7)	1 (8.3)	2 (16.7)	14 (28.6)
Stage IV	0 (0.0)	1 (8.3)	0 (0.0)	1 (8.3)	2 (4.1)
Functional status, n (%)					
Class I	1 (7.7)	2 (16.7)	2 (16.7)	2 (16.7)	7 (14.3)
Class II	7 (53.8)	9 (75.0)	9 (75.0)	8 (66.7)	33 (67.3)
Class III	5 (38.5)	1 (8.3)	1 (8.3)	2 (16.7)	9 (18.4)
Class IV	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

ACR, American College of Rheumatology; MTX, methotrexate; RA, rheumatoid arthritis.

Supplementary Table 2. Adverse Reactions to Methotrexate Treatment (Safety Population; Each Patient Received 1 oral MTX administration, 1 MTXAI delivered to the abdomen, and 1 MTXAI delivered to the thigh)

	N*	Comments
Adverse events		
SAEs	2	• 1 fatal MI (study day 6): 79-year-old man with prior cardiac history (MTXAI 25 mg abdomen) • Sick sinus syndrome (after trial concluded): 72-year-old man with history of CAD (MTXAI 15 mg thigh)
At least 1 TEAE[†]	3	Fatigue, nausea, worsening of RA[‡]
Injection site reactions		
Erythema	2	Grade 1

*Number of patients.

[†]Excluding TEAEs classified as SAEs.

[‡]Also led to discontinuation.

CAD, coronary artery disease; MI, myocardial infarction; MTXAI, methotrexate auto-injector; SAE, serious adverse event; TEAE, treatment-emergent adverse event.